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The Official Journal of the American Academy of Neurology



**Neurology Publish Ahead of Print**

**DOI:10.1212/WNL.000000000207481**

## Global Barriers to the Diagnosis of Multiple Sclerosis: Data From the Multiple Sclerosis International Federation Atlas of MS, Third Edition

**Author(s):**

Andrew J. Solomon, MD<sup>1</sup>; Ruth Ann Marrie, MD, PhD<sup>2</sup>; Shanthi Viswanathan, MD<sup>3</sup>; Jorge Correale, MD<sup>4</sup>; Melinda Magyari, PhD<sup>5</sup>; Neil P. Robertson, MD<sup>6</sup>; Deanna R. Saylor, MD, MHS<sup>7</sup>; Wendy Kaye, PhD<sup>8</sup>; Lindsay Rechtman, DrPh<sup>8</sup>; Eunchan Bae, MS<sup>9</sup>; Russell Shinohara, PhD<sup>9</sup>; Rachel King<sup>10</sup>; Joanna Laurson-Doube, PhD<sup>10</sup>; Anne Helme, PhD<sup>10</sup>

**Corresponding Author:**

Andrew J. Solomon, andrew.solomon@uvm.edu

**Affiliation Information for All Authors:** 1. Larner College of Medicine at the University of Vermont, Department of Neurological Sciences, Burlington, VT; 2. Departments of Internal Medicine and Community Health Science, Rady Faculty of Health Sciences, Max Rady College of Medicine, University of Manitoba, Winnipeg, MB, Canada; 3. Department of Neurology, Kuala Lumpur Hospital, Malaysia; 4. Departamento de Neurologia, Fleni, Buenos Aires, Argentina. Institute of Biological Chemistry and Physical Chemistry (IQUIFIB), National Council for Scientific and Technical Research/ University of Buenos Aires, Buenos Aires, Argentina; 5. Department of Neurology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark; 6. Department of Neurology, Division of Psychological Medicine and Clinical Neuroscience, Cardiff University, University Hospital of Wales, Cardiff, UK; 7. Department of Neurology, Johns Hopkins University School of Medicine, Baltimore MD USA; Department of Internal Medicine, University Teaching Hospital, Lusaka, Zambia; 8. McKing Consulting Corporation, Atlanta, GA, USA; 9. Department of Biostatistics, Epidemiology, and Informatics, Perelman School of Medicine, University of Pennsylvania, Philadelphia PA; 10. Multiple Sclerosis International Federation, London, UK

**Equal Author Contribution:**

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**Contributions:**

Andrew J. Solomon: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data

Ruth Ann Marrie: Drafting/revision of the manuscript for content, including medical writing for content; Study concept or design; Analysis or interpretation of data

Shanthi Viswanathan: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data

Jorge Correale: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data

Melinda Magyari: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data

Neil P. Robertson: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data

Deanna R. Saylor: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data

Wendy Kaye: Drafting/revision of the manuscript for content, including medical writing for content; Study concept or design; Analysis or interpretation of data

Lindsay Rechtman: Drafting/revision of the manuscript for content, including medical writing for content; Study concept or design; Analysis or interpretation of data

Eunchan Bae: Drafting/revision of the manuscript for content, including medical writing for content; Analysis or interpretation of data

Russell Shinohara: Drafting/revision of the manuscript for content, including medical writing for content; Study concept or design; Analysis or interpretation of data

Rachel King: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data

Joanna Laurson-Doube: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data

Anne Helme: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data

**Figure Count:**

5

**Table Count:**

1

**Search Terms:**

[ 41 ] Multiple sclerosis, [ 355 ] Health disparities, [ 335 ] All global neurology, [ 336 ] Access to care, Diagnosis

**Acknowledgment:****Study Funding:**

Multiple Sclerosis International Federation (MSIF) is an alliance of national multiple sclerosis (MS) organizations. MSIF receives income from a wide range of sources, including healthcare and other companies, individuals, member organizations, campaigns, foundations and trusts. Over the last 5 years, MSIF received funding from the following companies: Biogen, Bristol Myers Squibb, Janssen, Sanofi, Merck, Mylan, Novartis, and Roche – all of which is publicly disclosed.

**Disclosure:**

A.J. Solomon participates in contracted Research with Sanofi, Biogen, Novartis, Actelion, Genentech/Roche. Research support from Bristol Myers Squibb. Personal compensation for consulting for Genentech, Biogen, Alexion, Celgene, Greenwich Biosciences, Horizon Therapeutics, TG Therapeutics and Octave Bioscience. Personal compensation non-promotional speaking for EMD Serono. Expert witness testimony. R.A. Marrie receives research funding from: CIHR, Research Manitoba, Multiple Sclerosis Society of Canada, Multiple Sclerosis Scientific Foundation, Crohn's and Colitis Canada, National Multiple Sclerosis Society, CMSC, the Arthritis Society and US Department of Defense. SHE is a co-investigator on a study partially funded by Biogen Idec and Roche (no funds to her or her institution). She is supported by the Waugh Family Chair in Multiple Sclerosis. S. Viswanathan participates in contracted research with Alexion, Novartis, Sanofi and Roche. J. Correale has received financial compensation for academic presentations, assistance to advisory boards,

financial support for clinical and basic research, travel assistance to congresses from the following companies: Biogen, Merck, Novartis, Roche, Bayer, Sanofi-Genzyme, Gador, Raffo, Bristol Myers Squibb, and Janssen. M. Magyari has served in scientific advisory board for Sanofi, Novartis, Merck, and has received honoraria for lecturing from Biogen, Merck, Novartis, Roche, Genzyme, Bristol Myers Squibb. N. Robertson has received honoraria and/or support to attend educational meetings from Biogen, Novartis, Janssen, Genzyme, Roche. His institution has also received research support from Biogen, Novartis and Sanofi. D. Saylor has received funding from the National Multiple Sclerosis Society. W. E. Kaye – receives funding from the Agency for Toxic Substances and Disease Registry, the National Multiple Sclerosis Society, the Association for the Accreditation of Human Research Protection Programs, and Rockefeller University. L. Rechtman has no disclosures to report. E. Bae has no disclosures to report. R. T. Shinohara receives consulting income from Octave Bioscience, and compensation for scientific reviewing from the American Medical Association, the National Institutes of Health, the Department of Defense, and the Emerson Collective. R. King has no disclosures to report. J. Laurson-Doube has no disclosures to report. A. Helme has no disclosures to report.

**Preprint DOI:**

**Received Date:**

2022-09-22

**Accepted Date:**

2023-04-18

**Handling Editor Statement:**

Submitted and externally peer reviewed. The handling editors were Deputy Editor Bradford Worrall, MD, MSc, FAAN and Assistant Editor Amy Kunchok, MBBS, MMed, FRACP.

**Abstract:**

**Background and Objectives:** Recent data suggest increasing global prevalence of multiple sclerosis (MS). Early diagnosis of MS reduces the burden of disability-adjusted life years and associated healthcare costs. Yet diagnostic delays persist in MS care, and even within national healthcare systems with robust resources, comprehensive registries, and MS subspecialist referral networks. The global prevalence and characteristics of barriers to expedited MS diagnosis, particularly in resource-restricted regions, have not been studied extensively. Recent revisions to MS diagnostic criteria demonstrate potential to facilitate earlier diagnosis, but global implementation remains largely unknown.

**Methods:** The Multiple Sclerosis International Federation (MSIF) third edition of the Atlas of MS was a survey that assessed the current global state of diagnosis including: adoption of MS diagnostic criteria; barriers to diagnosis with respect to the patient, health care provider, and health system; and existence of national guidelines or national standards for speed of MS diagnosis.

**Results:** Coordinators from 107 countries (representing approximately 82% of the world population), participated. 83% reported at least one “major barrier” to early MS diagnosis. The most frequently reported barriers included: “lack of awareness of MS symptoms among general public” (68%) “lack of awareness of MS symptoms among healthcare professionals” (59%), and “lack of availability of “healthcare professionals with knowledge to diagnose MS” (44%). One-third reported lack of “specialist medical equipment or diagnostic tests”. 34% reported use of only 2017 McDonald criteria (McD-C) for diagnosis and 79% reported 2017 McD-C as the “most commonly used criteria”. 66% reported at least one barrier to adoption of 2017 McD-C, including “neurologists lack awareness or training” by 45%. There was no significant association between national guidelines pertaining to MS diagnosis or practice standards addressing speed of diagnosis and the presence of barriers to early MS diagnosis and implementation of 2017 McD-C.

**Discussion:** This study finds pervasive consistent global barriers to early diagnosis of MS. While these barriers reflected a lack of resources in many countries, the data also suggest that interventions designed to develop and implement accessible education and training can provide cost-effective opportunities to improve access to early MS diagnosis.

## Introduction

Recent data suggest an increasing global prevalence of multiple sclerosis (MS).<sup>1-6</sup> Revisions to the MS diagnostic criteria<sup>7</sup> over the last two decades have facilitated earlier diagnosis,<sup>8-10</sup> by obviating the need to wait for a second clinical event to diagnose MS. For example, in a cohort of 785 persons with MS from 9 European centers, median time to diagnosis was 58.5 months based on a second clinical event, 13.0 months based on the 2010 McDonald diagnostic criteria, and 3.2 months based on the 2017 McDonald criteria.<sup>11</sup> Expedited diagnosis consequentially has resulted in earlier treatment, even based on differences in the 2010 and 2017 criteria<sup>8</sup>, that is associated with improved clinical outcomes for people with MS (PwMS).<sup>12-15</sup> Earlier diagnosis of MS carries the potential to ease the high global burden<sup>1</sup> associated with this disease through a reduction in disability-adjusted life years and associated healthcare cost.

Despite the importance of rapid diagnosis, diagnostic delays persist in MS care,<sup>16-19</sup> and even within national healthcare systems with robust resources, comprehensive registries, and MS subspecialist referral networks.<sup>20-22</sup> A variety of contextual factors related to the affected individual, the health system and policy likely contribute to delays between symptom onset and confirmed diagnosis of MS. The Anderson model of total patient delay<sup>23</sup> suggests that an individual needs to recognize bodily changes and appraise symptoms as warranting a need for care, then to obtain an appointment. That health care provider needs to appraise the individual, and determine that investigations and referrals are needed. The specialist (neurologist) must be accessible, and may need to complete additional investigations to confirm diagnosis.

The global prevalence and characteristics of barriers within this diagnostic pathway that prevent expedited MS diagnosis, particularly in resource-restricted regions, have not been studied extensively. Moreover, the success of global dissemination and implementation efforts surrounding revisions to MS diagnostic criteria in particular remains largely unknown. Scant “real world” data limited to the United Kingdom and the United States continue to highlight miscomprehension and lack of implementation of contemporary criteria.<sup>24-26</sup>

This study aimed to synthesize novel global data focused on MS diagnosis collected as part of the recently completed Multiple Sclerosis International Federation’s (MSIF) third edition of the Atlas of MS - a worldwide study of the epidemiology of MS and the global availability and accessibility of diagnostic and clinical resources for PwMS. We report data focused on barriers to MS diagnosis, including the implementation of contemporary MS diagnostic criteria, that had been incorporated into the Atlas of MS for the first time (**Figure 1**). We further analyze the influence of World Bank category, World Health Organization Region, the presence of national standards surrounding MS diagnosis, and the presence of national guidelines focused on MS diagnosis, on barriers to diagnosis. This data from 107 countries representing 82% of the world’s population carries the potential to inform future clinical, educational, and healthcare policy - derived interventions aimed to improve early and accurate diagnosis of MS.

## Methods

This cross-sectional study conforms to CROSS reporting guidelines.

### *Setting*

The aim of the Atlas was to provide comprehensive understanding of the global burden of MS. This open source data is intended as a tool to: highlight disparities and inequalities, raise disease awareness, encourage improvements in surveillance systems and service provisions, inform and evidence advocacy efforts, and support the development of public policy to optimize the quality of life of people living with MS. The first edition of the Atlas of MS was published in 2008 in collaboration with the World Health Organization (WHO). The data was updated by MSIF in 2013 (second edition) and the third edition was launched in 2020-2. Data is collected by questionnaire. The third edition surveyed key epidemiological findings, and barriers and inequalities in relation to diagnosis, access to disease modifying therapies, and rehabilitation and symptom management.

## *Questionnaire Development*

The Atlas questionnaire was designed through an iterative process, by an Atlas working group comprised of MSIF members (MS organizations from 12 countries) and a panel of 16 Atlas expert advisors from 15 countries. These two groups included representation from all six World Health Organization regions,<sup>15</sup> all four World Bank (WB) economy income categories,<sup>27</sup> and specific expertise for the data collected. The MSIF International Working Group on Access and the MSIF International Medical and Scientific Board provided further review of the questionnaire. These groups were comprised of a range of stakeholders including clinicians, researchers, epidemiologists, volunteers/staff of MS organizations, and people affected by MS. Epidemiologists from McKing Consulting Corporation provided consultation regarding methodology, questionnaire design, data collection, and analyses.

Initially, important issues potentially affecting MS diagnosis and care in each region were identified by the Atlas working group. Second, the group reviewed questions from the second edition of the Atlas for relevance to these issues. Relevant questions were retained or modified to conform to the updated priorities of the third edition. Third, the questions, drafted in English, were reviewed for clarity by the MSIF staff and consultants, the Atlas Working Group, Atlas Expert Advisors, and the MSIF International Working Group for Access.

A finalized draft was converted to an online survey tool incorporating skip logic using SurveyMonkey.com for pilot testing. The questionnaire was then pilot tested by country coordinators from five countries (Argentina, Australia, India, Singapore, and Zambia) representing different WHO regions, WB income groups, and healthcare systems. No changes were made as a result of the pilot evaluation.

In collaboration with Guildhawk, a language and technology company, the questionnaire was translated and reviewed by a qualified native-speaking linguist in French and Spanish. An independent linguist proofread the translated files for additional quality assurance, and an additional review by Guildhawk staff was performed to check for accuracy. Each translation provided by Guildhawk was subsequently independently verified by a native French and a native Spanish speaker drawn from the Atlas working group and its expert advisors. This resulted in minor changes to the translated text before finalization and distribution to country coordinators through an electronic Word document. During this process, the text was not translated back to English from French or Spanish before dissemination.

The final subsection of the questionnaire (available as supplementary material, eAppendix 1) relating to the data presented in this paper included 13 questions that assessed: the current state of diagnosis including adoption of MS diagnostic criteria; barriers to diagnosis with respect to the patient, health care provider, and health system; and existence of national guidelines or national standards for MS diagnosis (including specifically speed of diagnosis). A glossary of terms was included within each question. Sources of data reported were also queried.

### *Standard Protocol Approvals, Registrations, and Patient Consents*

The Atlas of MS study methodology and questionnaire was not reviewed or approved by an institutional review board - this study surveyed healthcare professionals.

### *Questionnaire Distribution*

International contacts were identified through MSIF's network of MS organizations, the MSIF International Medical and Scientific Board, International Working Group on Access, previous Atlas contacts, the World Federation of Neurology, the Atlas working group and expert advisors, regional International Committees for the Treatment and Research in Multiple Sclerosis, as well as from scientific literature. Country coordinators, typically representatives from MS organizations, neurologists, epidemiologists, or researchers, were identified in each country and subsequently asked to complete the questionnaire while making use of all possible sources of information available to them including collaborating with other experts in the country where possible or necessary. Country coordinators were identified for 138 countries, and were queried regarding preferred questionnaire language; 123/138 (89.1%) requested English, 9 requested French, and 6 requested Spanish.

Data were collected between October 2019 and April 2020 via the online survey tool and country coordinators were provided electronic PDF or Word documents to allow collaboration and verification of the data with other experts.

## Analysis

Descriptive statistics are reported. For analyses WB High-income and Upper Middle-income categories were merged to create a High/Upper Middle-income category, and Lower Middle-income and Low-income were combined to create a Lower Middle/Low-income category due to sample size limitations.

The independent variables of interest were: (i) Use of McDonald 2017 criteria (yes/no, Not sure excluded); (ii) most commonly use McDonald 2017 criteria (yes/no, Not sure was excluded); the presence of at least one major barrier to early diagnosis of MS (yes/no, Not sure was excluded). The outcomes of interest were: (i) any national standards or targets set relating to the diagnosis, treatment or monitoring of MS patients in the country (yes/no); (ii) any national guidelines for diagnosis, treatment or living with MS? (yes/no); (iii) speed of diagnosis as a standard (yes/no).

We conducted a Fisher's exact test to test the association between the survey responses for these variables and WB income categories or WHO regions as well as the unadjusted association between two survey responses.

We used a series of multivariable logistic regression models to test the associations between the independent variables and outcomes of interest while adjusting for WB income and WHO region. We report the generalized variance inflation factor (gVIF)<sup>28</sup> to test the multicollinearity of WB income and WHO regions, C-statistics to test discriminating ability, and p-value of Hosmer-Lemeshow Goodness of Fit (GOF) test to test the model fit (**eTable 1**).<sup>29</sup> A c-statistic of 0.5 indicates the model is no better than chance at predicting the outcome, and 1.0 indicates perfect classification. A p-value for the GOF test of >0.05 indicates a good fit.

All statistical analysis was conducted in R 4.0.2 (<https://www.R-project.org/>.) Data are available upon request to MSIF.

## Results

Coordinators representing one hundred and seven countries (approximately 82% of the world population), participated in the section of the Atlas questionnaire focused on MS diagnosis (**Figure 2, and eTables 2 and 3**). Descriptive open-source data are available from MSIF (<https://www.atlasofms.org>). Data generated by each country coordinator completing the survey comprise the reported results from each country.

### Current State of MS Diagnosis

The type of source consulted by country coordinators to provide information on diagnostic criteria included a published academic paper or poster: 51/107 (48%), patient data: 54/107 (50%), personal opinion: 72/107 (67%), opinion of others: 45/107 (42%), other: 3/107 (3%).

**Figure 3** details responses to the three questions surrounding MS diagnostic criteria. Schumacher (1965), Poser (1983), and McDonald criteria (McD-C) and its revisions (2001, 2005, 2011, 2017) all currently remained in use. Thirty-six (34%) countries reported using only 2017 McD-C for diagnosis. WB High/Upper Middle-income countries were more likely (n=31, 42%) than Lower Middle/Low-income countries (n=5, 16%) (p = 0.007) to report using only 2017 McD-C for diagnosis compared to any McD-C, while there was no difference by WHO region (p = 0.13). Two countries (Burundi, Morocco) reported not using any McD-C criteria.

The 2017 McD-C were reported as the "most commonly used criteria" to diagnose MS in 84 (79%) countries, and this was more likely in WB High/Upper Middle-income countries than WB Lower Middle/Low-income countries (66 [90%] vs. 18 [58%], p<0.001) but did not differ by WHO region (p = 0.31).

Procedures reported as used for the diagnosis of MS included neurological examination by 106/106 (100%), MRI by 103/106 (97%), Spinal tap by 96/106 (91%), Evoked potentials by 69/106 (65%), Optical Coherence Tomography by 40/106 (38%), and other by 5/106 (5%). MRI was not reported as a procedure used to diagnose MS in 3 (3%) countries (Burundi, Central African Republic, and Malawi).

## Barriers to Diagnosis

Sources consulted by country coordinators surrounding barriers to diagnosis included published academic articles or posters 30/106 (82%), patient data 57/106 (54%), personal opinion 81/106 (76%), opinion of others 54/106 (51%), and other: 3/106 (3%).

Over eighty percent (n=88) of countries reported at least one “major barrier” to early MS diagnosis (**Figure 4**). From the patient perspective (of symptom appraisal and care seeking), the most frequently reported barrier was “lack of awareness of MS symptoms among general public” by 72 (68%). From the health care provider perspective, the most commonly reported barrier was “lack of awareness of MS symptoms among healthcare professionals” (n=63, 59%). This barrier was closely related to a lack of availability of “healthcare professionals with knowledge to diagnose MS” (n=47, 44%). Of the countries reporting a lack of knowledgeable health professionals, 38 (88%) reported specialist MS neurologists are “not readily available” and 26 (60%) reported neurologists are “not readily available”. This problem was compounded by a lack of “specialist medical equipment or diagnostic tests” in one-third of countries (n =36). Of those countries, 24 (69%) reported MRI machines, and 27(77%) reported “specialist laboratory equipment/tests for accurate diagnosis” are “not readily available”.

WB Lower Middle/Low-income countries reported at least one major barrier preventing early MS diagnosis more frequently than WB High/Upper Middle-income countries (31 [94%] vs. 57 [78%],  $p = 0.05$ ) while there were no significant differences between WHO regions ( $p = 0.09$ ).

Sixty-six (66%) countries reported at least one barrier to adoption of 2017 McD-C, most often that “neurologists lack awareness or training” (n = 45, 45%). WB Lower Middle/Low-income countries reported at least one barrier to adoption of 2017 McD-C more often than WB High/Upper Middle-income countries (29 [88%] vs. 37 [51%]  $p<0.001$ ). Europe (19 [46%]) and Eastern Mediterranean (9 [50%]) WHO regions were less likely to report at least one barrier to adoption of 2017 McD-C compared to all other regions (Africa: 13 [87%], America: 13 [76%], Western Pacific: 7 [78%], South East Asia: 5 [83%]) ( $p<0.001$ ).

## Guidelines or National Standards

Fifty-one (49%) countries reported having national guidelines that cover diagnosis of MS (**Figure 5**). WB High/Upper Middle-income countries reported national guidelines covering diagnosis of MS more often than WB Lower Middle/Low-income countries (45 [63%] vs. 6 [18%],  $p<0.001$ ). Europe and Eastern Mediterranean WHO regions were more likely to report national guidelines covering diagnosis of MS than all other WHO regions (33 [56%] vs. 18 [36%]  $p<0.001$ ).

Forty-three (41%) countries reported national standards pertaining to MS care, and of those, 24 (56%) countries reported standards for “speed of diagnosis”. WB High/Upper Middle-income countries also reported national standards more frequently than WB Lower Middle/Low -income countries (36/73 [49%] vs. 7/31 [18%],  $p = 0.016$ ). National standards pertaining to MS was also associated with WHO region ( $p<0.001$ ). Europe and Eastern Mediterranean WHO regions were more likely to report such national standards compared to all other WHO regions (35 [59%] vs. 8 [18%],  $p<0.001$ ).

Countries reporting “only using McD-C 2017” had 77% reduced odds of having “national standards” (OR: 0.23 (95% CI: 0.07 – 0.68), c-statistic: 0.75, Hosmer-Lemeshow GOF p-value: 0.56), and 63% reduced odds of having “guidelines that cover diagnosis” (OR: 0.37 (95% CI: 0.13 – 1.01), only after adjusting for WB income category and WHO region (**Table 1 and eFigure1**). There was no significant association between countries reporting 2017 McD-C as the “most commonly” used criteria and the presence of diagnostic guidelines, before or after adjusting for WB income category and WHO region.

No statistically significant association was identified between countries reporting a “speed of diagnosis” standard and reporting only use of 2017 McD-C, before or after adjusting for WB income and WHO region (**Table 1**). There was also no association between countries reporting a “speed of diagnosis” standard and reporting 2017 McD-C as the “most commonly used” criteria, before or after adjusting for WB income and WHO region.

There was no significant association between countries with at least one barrier to early diagnosis and guidelines that cover diagnosis, before or after adjusting for WB income and WHO region. There was no

statistically significant association between countries with at least one barrier to early diagnosis and the presence of national standards, before or after adjusting for WB income and WHO region (**Table 1**).

## Discussion

We investigated the presence and characteristics of healthcare system barriers to MS diagnosis in 107 countries. Eight in ten participating countries reported at least one “major barrier” to MS diagnosis and six in ten reported at least one barrier to the adoption of 2017 McD-C, and frequent concurrent use of prior less sensitive diagnostic criteria. We found that there were barriers to timely diagnosis that were pervasive throughout the entire patient journey – ranging from lack of patient awareness, to lack of health care provider awareness and knowledge/training, to lack of personnel and infrastructure to implement recommendations around diagnosis even if the knowledge and awareness were available.

Barriers to timely MS diagnosis reflected a lack of resources in many countries. This most often included a lack of healthcare professionals, including neurologists and subspecialty MS neurologists in particular, and medical equipment or diagnostic tests such as MRI machines, and other laboratory equipment, particularly in lower-income settings. In addition, people suspected of having MS often did not complete recommended testing due to cost and/or related required travel, indicating that health care disparities likely play an important role in delayed diagnoses. Compared to 94% of WB High/Upper Middle-income countries, only 58% of Lower Middle/Low-income countries reported 2017 McD-C as the most commonly used diagnostic criteria, which may reflect a lack of trained healthcare professionals or other barriers to implementation at the health system level. WB Lower Middle/Low-income countries were more affected by a lack of resources, and were more likely to report at least one major barrier preventing early MS diagnosis, with almost every country (94%) reporting such. By contrast, these differences were not found with respect to WHO region. Improving the availability and accessibility of resources in these regions is likely to be complex and challenging, requiring country-specific interventions. However, efforts such as the development of laboratory testing utilizing dried blood spots<sup>30</sup> and portable low field MRI sensitive to MS lesions<sup>31</sup> show promise to reduce cost and travel-associated barriers to timely evaluation of possible MS diagnoses in resource-limited regions.

Importantly, the data also suggest that interventions designed to develop and implement accessible education and training may provide cost-effective opportunities to improve access to early MS diagnosis. Lack of healthcare provider awareness or training were frequently reported barriers to early MS diagnosis and to the adoption of contemporary McD-C. Interventions leveraging resources already in place may improve access to early diagnosis. For instance, telemedicine may provide accessible and cost-effective opportunities for education, training and direct care in resource limited regions. A recent study demonstrated that teleneurology visits were feasible and acceptable for adult patients attending an outpatient neurology clinic in Zambia, while reducing expense and time associated with care.<sup>32</sup> Telemedicine may also be implemented to train regional clinicians in MS diagnosis and care<sup>33</sup>, who can subsequently serve as experts leading educational outreach efforts while providing subspecialist level telemedicine consultations for local providers in their region. Once such efforts are successful, outreach to increase awareness among primary care providers and other non-neurologist physicians who may first encounter patients with symptoms suggestive of MS (e.g. ophthalmologists) along with the development of efficient referral networks is necessary. In spite of accessible and available care for early MS diagnosis in some regions, a lack of awareness of MS symptoms among the general public was also frequently reported – a barrier also amenable to educational efforts where models from other chronic disease interventions such as engaging mass media, faith-based institutions, and advocacy services, may be informative.<sup>34</sup>

Although data support earlier diagnosis and improved outcomes in patients with MS as a result of revisions to MS diagnostic criteria over the last twenty years, there is scant literature concerning global implementation.<sup>24, 25</sup> This study highlights delay in widespread adoption of revised 2017 McD-C approximately 21 to 27 months after publication. Although a majority of countries reported that 2017 McD-C was the most commonly used criteria, many also reported continued use of prior criteria as part of routine care, suggesting heterogeneous practice in these regions. Persistent utilization of earlier criteria may unnecessarily delay diagnosis in contrast to comparably more sensitive contemporary criteria in a small but significant group of patients.<sup>8</sup> Approximately half WB High/Upper Middle-income countries reported at least one barrier to adoption of 2017 McD-C, including 10% who did not report that 2017 McD-C was the most commonly used diagnostic



criteria. This suggests that resource limitations were not the sole cause of delayed adoption of 2017 McD-C - improved dissemination and parallel education efforts should accompany any future revisions to MS diagnostic criteria to improve global implementation.

This study had limitations. Few peer-reviewed publications exist on the availability of and access to MS diagnosis in many countries, and as a result, this study relied on expert opinion in the absence of such data. These data may therefore also not capture heterogeneity and unmeasured contextual factors that may influence MS diagnosis in each country. Future studies in these regions might pursue evaluation of administrative or direct clinical data to verify and better characterize these findings where possible. However, to improve confidence in these data, collaborations between country coordinators and other experts were requested as well as the enumeration of data sources consulted if available. Most participating countries referenced the independent evidence consulted (academic papers or patient data such as surveys or registries) rather than reliance on opinion alone. A future Atlas effort may consider directly collecting and assessing the evidence used to inform responses, as well as any barriers to its availability experienced by country coordinators. Funding to support for the development of MS registries in resource-limited regions may expand global representation and increase quantitative country-specific data for future studies evaluating barriers to MS diagnosis. Engagement with regional clinicians, MS advocacy groups, and public awareness campaigns would be needed to aid development and ensure the success of such initiatives. However, efforts toward population surveillance of other diseases<sup>35</sup> in low-income to middle income countries suggest that single region or country-specific registries alone may be inadequate, and that optimal approaches to comprehensive surveillance of MS will likely require leveraging multiple sources of regional health data as well as international collaboration.

In this study there was under-representation of countries from the African WHO region and countries classified as WB low-income (**eTables 2 and 3**) and the present data therefore likely underestimates barriers to early MS diagnosis across these regions. This partly reflects the consequences of a severe lack of neurologists. For example, the number of neurologists in WHO Africa region is an estimated median of 0.04 per 100,000 people (compared to 6.6 in Europe).<sup>36</sup> Many countries in Africa have 0, or 1-2 neurologists providing care. The resulting burden of patient care, teaching, and administrative responsibilities may make such providers less able to participate in initiatives such as the Atlas of MS. Furthermore, such countries have few if any neurologists with subspecialty MS expertise or capability to focus on MS given neurological care necessitated more broadly and by more prevalent neurological conditions. In regions with few providers of neurological care, knowledge for neurology is often further limited among non-neurologists, making recognition of symptoms of MS and referral to a neurologist even less likely. As a result, there are scant data concerning MS prevalence and care in Africa.<sup>37</sup>

Methodology employed for the Atlas provides an overall estimate of barriers to early MS diagnosis in these regions but limits detailed assessments or conclusions regarding accurate or early diagnosis within or between regions. For instance, as recent data in the US have highlighted, adoption of McD-C does not necessarily ensure accurate comprehension and application of its key elements.<sup>26</sup> Similarly, despite few diagnostic barriers reported by some countries, social determinants of health and other factors may still create inequalities influencing healthcare access to facilitate early MS diagnosis for some patients.<sup>38</sup> Further country-specific quantitative data concerning MS diagnosis are needed to better understand the experience of patients in these regions. Importantly, data collection was completed in April 2020, and as a result would not have adequately captured any impact of the COVID-19 pandemic on MS diagnosis.

This study finds pervasive consistent global barriers to early diagnosis of MS. International expert consensus efforts have repeatedly affirmed optimal diagnostic approaches and the importance of early diagnosis to improve clinical outcomes in MS.<sup>7, 39, 40</sup> The challenges of dissemination of research findings, practice guidelines, and diagnostic criteria, particularly in resource-limited regions, are well-documented.<sup>41-43</sup> Indeed, this study found little association between national guidelines or standards for MS care and fewer barriers to early diagnosis. The development and improvement of much needed healthcare system resources required to ameliorate global barriers to MS diagnosis will necessitate difficult policy initiatives. Despite these issues, these data present a key opportunity to improve and expedite diagnosis of MS in many worldwide regions through provider and patient-focused educational interventions. Such approaches, incorporated in policy initiatives such as the recently WHO adopted Intersectoral Global Action Plan on Epilepsy and Other Neurological Disorders 2022–2031,<sup>44</sup> optimize clinical resources that are already in place. Models implemented

by organizations such as the World Federation of Neurology<sup>45</sup> and others<sup>33, 46-49</sup> to assess and develop worldwide neurology-focused educational resources and programs, particularly in resource-limited regions, should be considered.

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**Table 1.** Odds ratios (95% confidence intervals) for associations between use of the McDonald 2017 criteria and national standards or diagnostic guidelines for multiple sclerosis before and after adjustment for World Bank income and World Health Organization region

|  | National standards <sup>4</sup> |                       | Diagnostic guidelines <sup>5</sup> |                      | Speed of diagnosis Standard <sup>6</sup> |                       |
|--|---------------------------------|-----------------------|------------------------------------|----------------------|--|-----------------------|
|  | Unadjusted                      | Adjusted              | Unadjusted                         | Adjusted             | Unadjusted                               | Adjusted              |
| Only use McD-C 2017 <sup>1</sup>               | 0.68<br>(0.27, 1.68)            | 0.24*<br>(0.07, 0.68) | 0.78<br>(0.32, 1.89)               | 0.37<br>(0.13, 1.01) | 1.39<br>(0.31, 6.75)                     | 2.71<br>(0.59, 14.04) |
| Most commonly use McD-C2017 <sup>2</sup>       | 1.77<br>(0.56, 6.27)            | 0.74<br>(0.18, 2.89)  | 1.40<br>(0.46, 4.47)               | 0.38<br>(0.08, 1.49) | 0.60<br>(0.05, 4.76)                     | 0.27<br>(0.005, 4.80) |
| At least one barrier to diagnosis <sup>3</sup> | 0.50<br>(0.15, 1.57)            | 1.09<br>(0.34, 3.50)  | 0.72<br>(0.22, 2.23)               | 1.23<br>(0.38, 3.93) | 0.46<br>(0.07, 2.49)                     | 0.35<br>(0.006, 1.75) |

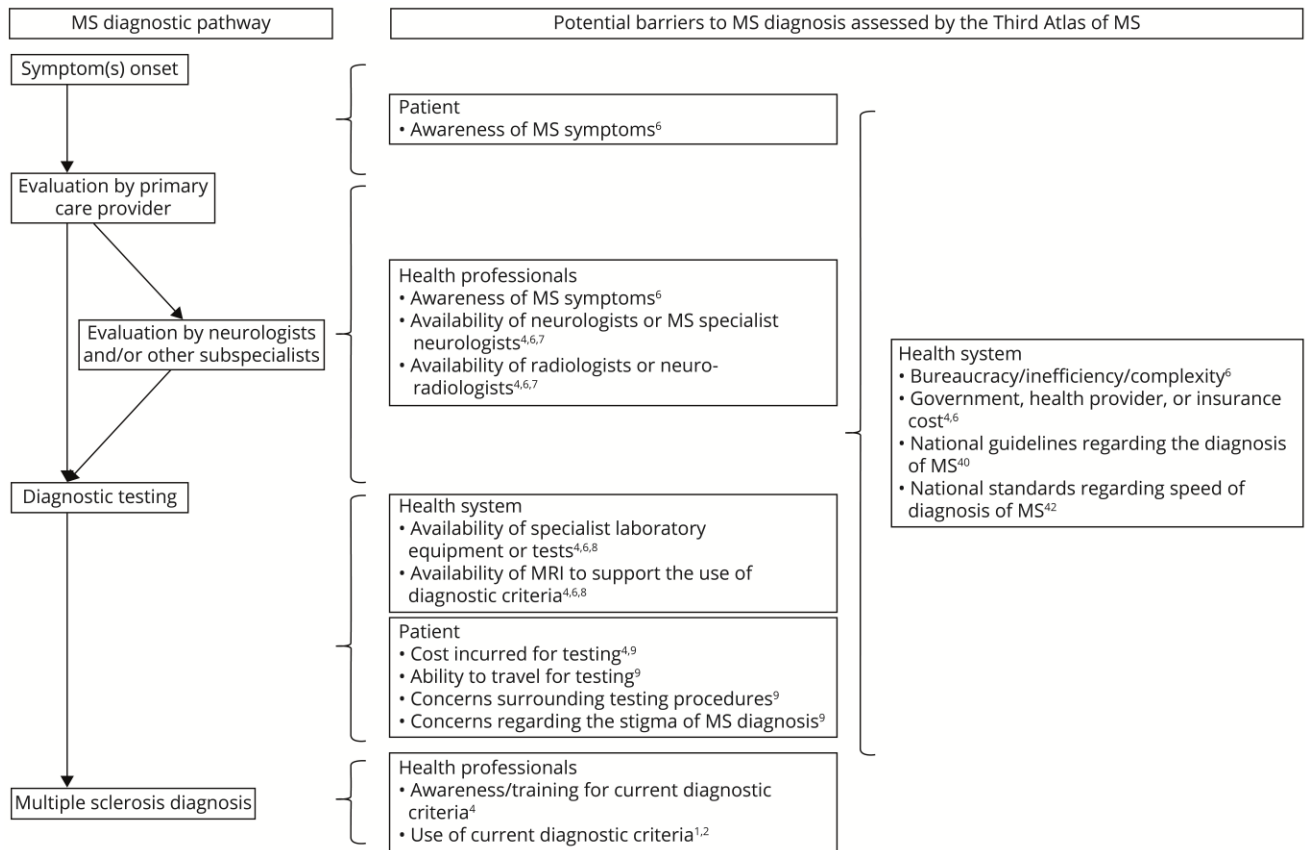
\*:  $p < 0.05$

- Confidence interval of the multivariate logistic regression is calculated using confint function in stats package in R.

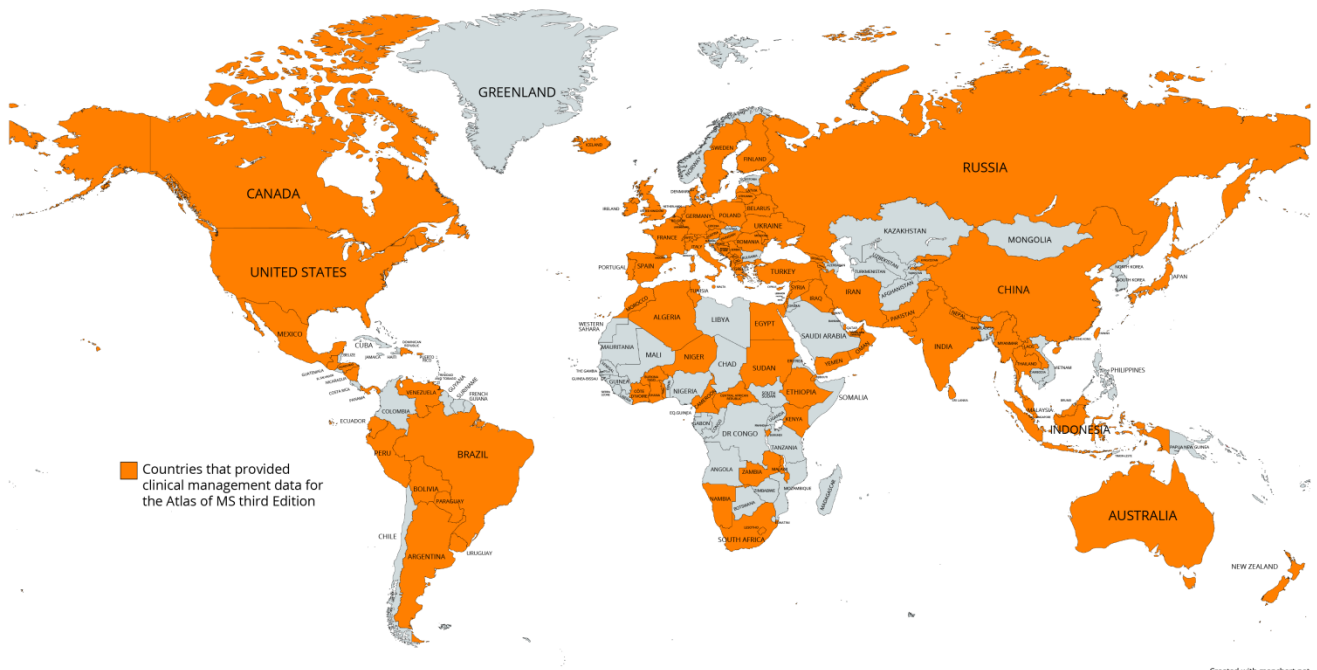
1. "Please indicate all the MS diagnostic criteria that you are aware are used in the country?". Responses are categorized as yes if "Yes" if "McDonald criteria – 2017 version" selected, and no if "No" if other criteria selected. "Not Sure" is excluded.
2. "And which ONE criteria do you think is currently the most commonly used to diagnose MS in the country?". Responses are categorized as yes if "McDonald criteria – 2017 version" selected, and no if other than "McDonald criteria – 2017 version" selected. "Not sure" is excluded.
3. "Please indicate the major barriers in the country that prevent individuals from receiving a MS diagnosis as early as possible. Please indicate all major barriers that apply". Responses are categorized as yes if "Yes" and no if "No". "Not sure" is excluded.
4. "Are there any national standards or targets set relating to the diagnosis, treatment or monitoring of MS patients in the country?". Responses are categorized as yes if "Yes" and no if "No".
5. "Does the country have any national health plan(s) or guidelines that cover aspects of diagnosis, treatment or living with MS? Please indicate all that apply." Selection of "Yes – diagnosis" are categorized as yes and no if "Yes – diagnosis" is no selected. "Not sure" is excluded.
6. "What aspects of the diagnosis, treatment or monitoring of MS patients in the country have targets or standards". Responses are categorized as yes if "Speed of diagnosis" selected and no if "Speed of diagnosis" unchecked.

**Figure 1: Potential patient, health professional, and healthcare system-related barriers on the diagnostic pathway to MS assessed by the Third Atlas of MS.**

Superscript numbers indicate the Atlas question number that assessed each specific potential barrier to diagnosis.



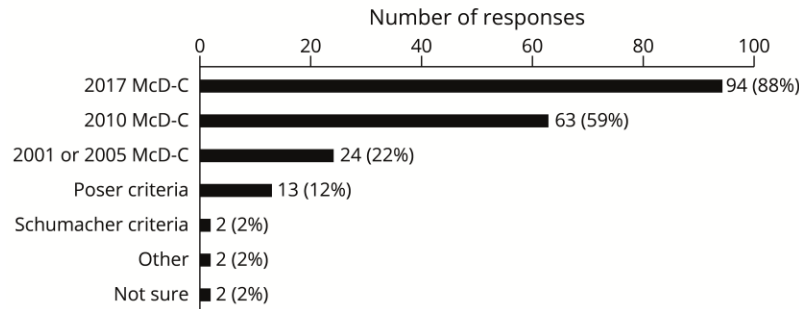
**Figure 2: Countries that provided clinical management data for the Atlas of MS Third Edition.**



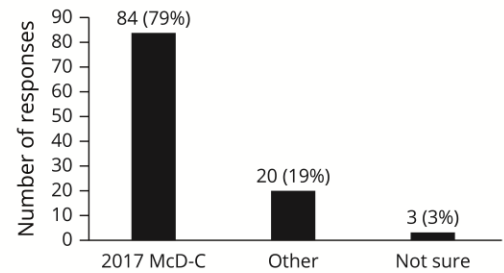
**Figure 3: Use of MS diagnostic criteria**

A: Responses to the query for all MS diagnostic criteria currently used by providers (may select more than one response). B: Responses to a second question quering the “most commonly” used MS diagnostic criteria by providers, demonstrating the proportion indicating 2017 McDonald criteria. C: Responses regarding why 2017 McDonald criteria is not being used or not being used all the time by providers in the country (may select more than one response).

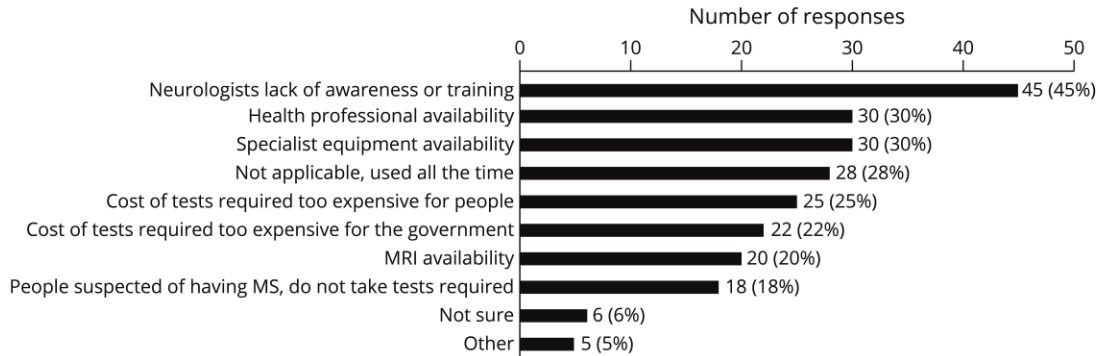
A. MS diagnostic criteria used: N (%)



B. Which one criterion is currently the most commonly used to diagnose MS?: N (%)



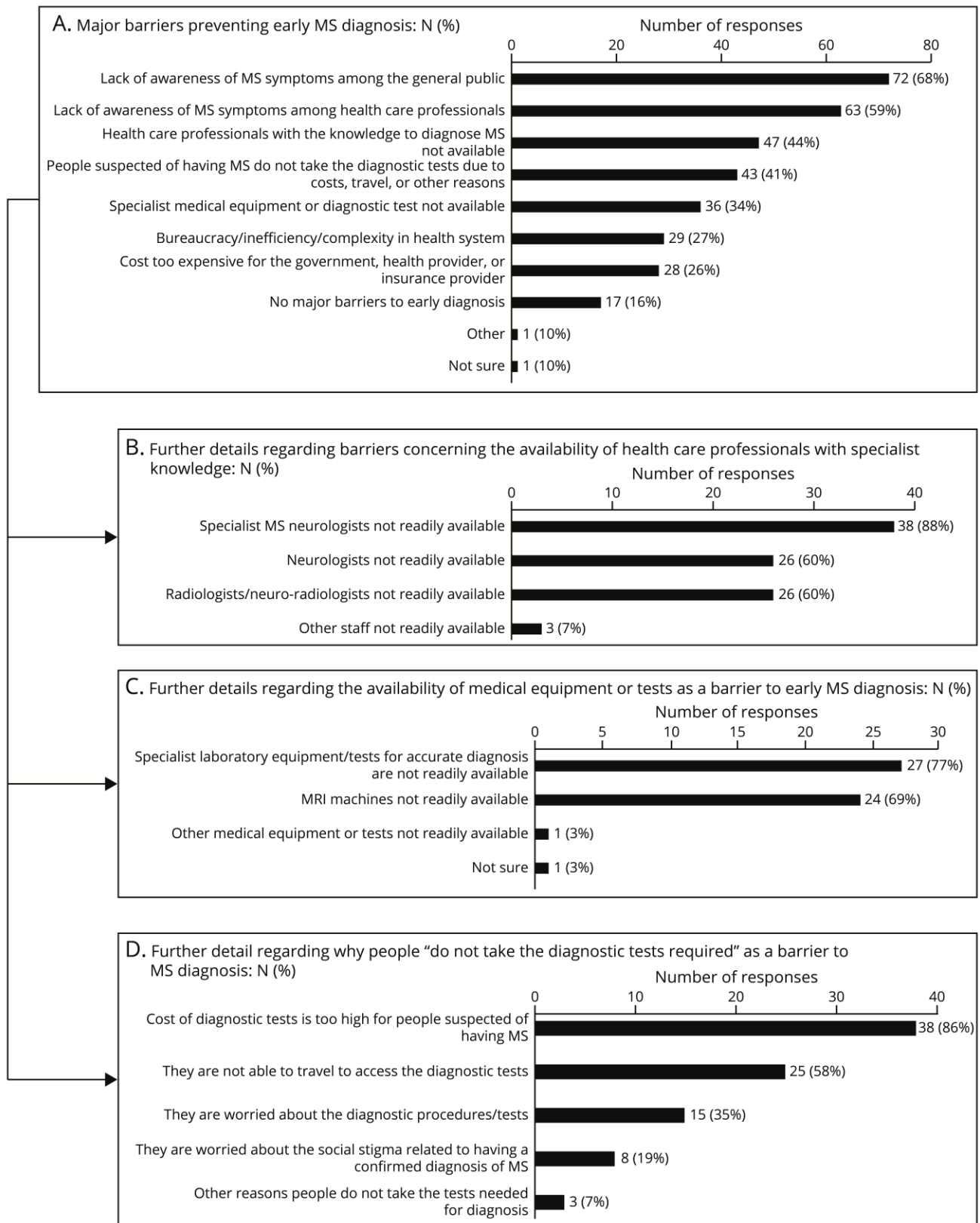
C. Why is the 2017 McDonald criteria not being used or not being used all the time by all neurologists in the country?: N (%)



**Figure 4: Major barriers to early MS diagnosis**

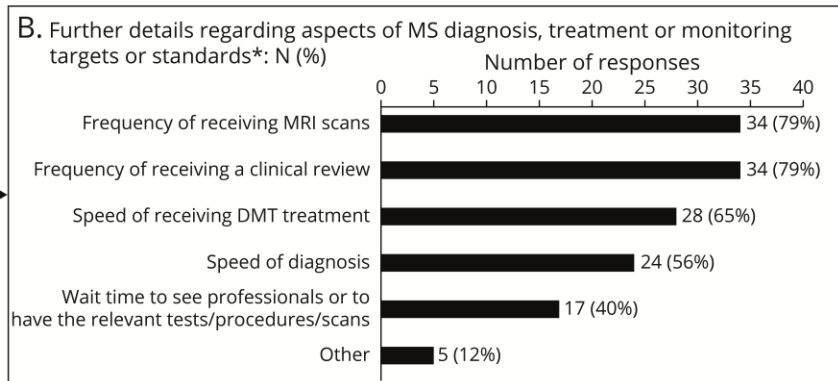
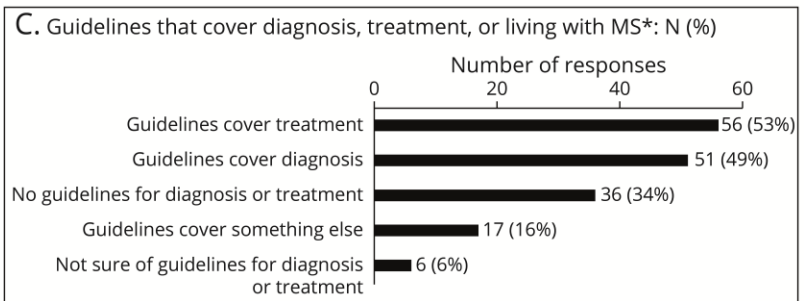
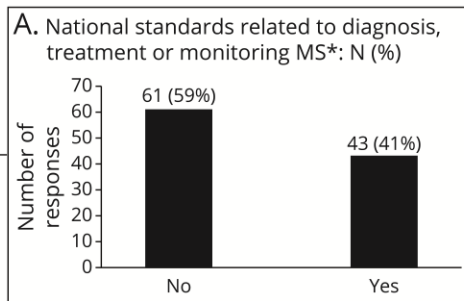
A: Responses to query regarding major barriers that prevent early diagnosis of MS (may indicate more than one), and further responses obtained in a follow up question if barriers involving the B: availability of “healthcare professionals with subspecialist knowledge”, C: “medical equipment or tests”, or D: “people do not take the diagnostic tests”, were selected.

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**Figure 5: National standards or guidelines relating to MS**

Proportion of responses indicating (A) national standards related to MS diagnosis, (B) national standards focused on speed of diagnosis of MS, or (C) the presence of national guidelines that cover diagnosis of MS.



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## Global Barriers to the Diagnosis of Multiple Sclerosis: Data From the Multiple Sclerosis International Federation Atlas of MS, Third Edition

Andrew J. Solomon, Ruth Ann Marrie, Shanthy Viswanathan, et al.

*Neurology* published online June 15, 2023

DOI 10.1212/WNL.0000000000207481

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